

Appl. No. 10/058,069
Amendment dated February 10, 2005
Reply to Non-Final Official Action of August 10, 2004
Attorney Ref. No.: 037003-0280727

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claims 20, 29, and 38 are amended, claims 1-19, 21-28, 30-37, and 41-50 are canceled, and new claims 51-79 are submitted.

1-19. (Canceled)

20. (Currently amended) A kit useful for the treatment of a mammal suffering from or predisposed to a neoplastic disorder comprising at least one container having a dimeric antibody that binds specifically to TAG-72 deposited therein,

which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer,

wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides and two antibody light chain polypeptides, and has two antigen-binding sites;

wherein one or more of the antigen binding sites of the tetravalent antibody dimer binds specifically to TAG-72; and

wherein a C_H2 domain is deleted from each of the four antibody heavy chain polypeptides in the dimeric antibody;

and further comprising a label or an insert indicating that said dimeric antibody may be used to treat said neoplastic disorder.

21-28. (Canceled)

29. (Currently amended) A dimeric antibody that binds specifically to TAG-72 ~~comprising a plurality of monomeric subunits~~

which dimeric antibody comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer,

wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides and two antibody light chain polypeptides, and has two antigen-binding sites;

wherein one or more of the antigen binding sites of the tetravalent antibody dimer binds specifically to TAG-72; and

wherein a C_H2 domain is deleted from each of the four antibody heavy chain polypeptides in the dimeric antibody

~~wherein said monomeric subunits are non-covalently associated.~~

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30-37. (Canceled)

38. (Currently amended) The dimeric antibody of claim 29 wherein said dimeric antibody is ~~associated with~~ conjugated to a cytotoxic agent.

39. (Original) The dimeric antibody of claim 38 wherein said cytotoxic agent comprises a radioisotope.

40. (Original) The dimeric antibody of claim 39 wherein said radioisotope is selected from the group consisting of ^{90}Y , ^{125}I , ^{131}I , ^{123}I , ^{111}In , ^{105}Rh , ^{153}Sm , ^{67}Cu , ^{67}Ga , ^{166}Ho , ^{177}Lu , ^{186}Re and ^{188}Re .

41-50. (Canceled)

New claims:

51. (New) The kit of claim 20, wherein the antigen-binding sites of one of the antibodies in the dimer bind specifically to the same epitopes as the antigen-binding sites of the other antibody in the dimer

52. (New) The kit of claim 20, wherein one of the antibodies in the dimer binds specifically to at least one epitope to which the other antibody in the dimer does not specifically bind.

53. (New) The kit of claim 20, wherein said antibody dimer comprises a humanized antibody that binds specifically to TAG-72 and comprises complementarity determining regions of a non-human anti-TAG-72 antibody and framework regions of a human antibody.

54. (New) The kit of claim 53, wherein said humanized antibody comprises complementarity determining regions of a non-human anti-TAG-72 antibody selected from the group consisting of: CC49 (ATCC No. HB 9459); CC83 (ATCC No. HB 9453); CC46 (ATCC No. HB 9458); CC92 (ATCC No. HB 9454); CC30 (ATCC No. HB 9457); CC11 (ATCC No. 9455); and CC15 (ATCC No. HB 9460).

55. (New) The kit of claim 20, wherein said antibody dimer comprises a chimeric antibody comprising light and heavy chain variable region polypeptides of a non-human antibody that bind specifically to TAG-72, and human antibody constant regions.

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56. (New) The kit of claim 20, wherein said antibody dimer comprises an antibody heavy chain polypeptide in which a C_H3 domain is fused directly to the hinge region.

57. (New) The kit of claim 20, wherein said antibody dimer comprises an antibody heavy chain polypeptide in which an amino acid spacer is inserted in place of a deleted C_H2 domain.

58. (New) The kit of claim 57, wherein the amino acid spacer has the amino acid sequence Gly-Gly-Ser-Ser-Gly-Gly-Gly-Gly-Ser-Gly (SEQ ID NO: 17).

59. (New) The kit of claim 20, wherein said antibody dimer comprises four antigen binding sites that bind specifically to TAG-72.

60. (New) The kit of claim 59, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain variable region amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain variable region amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

61. (New) The kit of claim 59, wherein said antibody dimer comprises four antibody heavy chain polypeptides in which a C_H3 domain is fused directly to a hinge region.

62. (New) The kit of claim 61, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

63. (New) The kit of claim 20 wherein said neoplastic disorder is colon cancer.

64. (New) The dimeric antibody of claim 29, wherein the antigen-binding sites of one of the antibodies in the dimer bind specifically to the same epitopes as the antigen-binding sites of the other antibody in the dimer

65. (New) The dimeric antibody of claim 29, wherein one of the antibodies in the dimer binds specifically to at least one epitope to which the other antibody in the dimer does not specifically bind.

66. (New) The dimeric antibody of claim 29, wherein said antibody dimer comprises a humanized antibody that binds specifically to TAG-72 and comprises complementarity

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determining regions of a non-human anti-TAG-72 antibody and framework regions of a human antibody.

67. (New) The dimeric antibody of claim 66, wherein said humanized antibody comprises complementarity determining regions of a non-human anti-TAG-72 antibody selected from the group consisting of: CC49 (ATCC No. HB 9459); CC83 (ATCC No. HB 9453); CC46 (ATCC No. HB 9458); CC92 (ATCC No. HB 9454); CC30 (ATCC No. HB 9457); CC11 (ATCC No. 9455); and CC15 (ATCC No. HB 9460).

68. (New) The dimeric antibody of claim 29, wherein said antibody dimer comprises a chimeric antibody comprising light and heavy chain variable region polypeptides of a non-human antibody that bind specifically to TAG-72, and human antibody constant regions.

69. (New) The dimeric antibody of claim 29, wherein said antibody dimer comprises an antibody heavy chain polypeptide in which a C_H3 domain is fused directly to the hinge region.

70. (New) The dimeric antibody of claim 29, wherein said antibody dimer comprises an antibody heavy chain polypeptide in which an amino acid spacer is inserted in place of a deleted C_H2 domain.

71. (New) The dimeric antibody of claim 70, wherein the amino acid spacer has the amino acid sequence Gly-Gly-Ser-Ser-Gly-Gly-Gly-Gly-Ser-Gly (SEQ ID NO: 17).

72. (New) The dimeric antibody of claim 29, wherein said antibody dimer comprises four antigen binding sites that bind specifically to TAG-72.

73. (New) The dimeric antibody of claim 72, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain variable region amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain variable region amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

74. (New) The dimeric antibody of claim 72, wherein said antibody dimer comprises four antibody heavy chain polypeptides in which a C_H3 domain is fused directly to a hinge region.

75. (New) The dimeric antibody of claim 74, wherein said antibody dimer comprises four antibody heavy chain polypeptides having the heavy chain polypeptide amino acid sequence shown in Figure 4A (SEQ ID NO: 7), and four antibody light chain polypeptides having the light chain polypeptide amino acid sequence shown in Figure 5A (SEQ ID NO: 9).

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76. (New) The dimeric antibody of claim 38, wherein said cytotoxic agent is selected from the group consisting of cytostatic agents, alkylating agents, antimetabolites, anti-proliferative agents, tubulin binding agents, hormones and hormone antagonists, anthracycline drugs, vinca drugs, mitomycins, bleomycins, cytotoxic nucleosides, pteridine drugs, diynenes, podophyllotoxins, toxic enzymes, and radiosensitizing drugs.

77. (New) The dimeric antibody of claim 76, wherein said cytotoxic agent is selected from the group consisting of mechlorethamine, triethylenephosphoramide, cyclophosphamide, ifosfamide, chlorambucil, busulfan, melphalan, triaziquone, nitrosourea compounds, adriamycin, carminomycin, daunorubicin (daunomycin), doxorubicin, aminopterin, methotrexate, methopterin, mithramycin, streptonigrin, dichloromethotrexate, mitomycin C, actinomycin-D, porfiromycin, 5-fluorouracil, floxuridine, ftorafur, 6-mercaptopurine, cytarabine, cytosine arabinoside, podophyllotoxin, etoposide, etoposide phosphate, melphalan, vinblastine, vincristine, leurosine, vindesine, leurosine, taxol, taxane, cytochalasin B, gramicidin D, ethidium bromide, emetine, tenoposide, colchicin, dihydroxy anthracin dione, mitoxantrone, procaine, tetracaine, lidocaine, propranolol, puromycin, ricin subunit A, abrin, diphtheria toxin, botulinum, cyanginosins, saxitoxin, shigatoxin, tetanus, tetrodotoxin, trichothecene, verrucologen, corticosteroids, progestins, estrogens, antiestrogens, androgens, aromatase inhibitors, calicheamicin, esperamicins, and dynemicins.

78. (New) The dimeric antibody of claim 76, wherein said hormone or hormone antagonist is selected from the group consisting of prednisone, hydroxyprogesterone, medroprogesterone, diethylstilbestrol, tamoxifen, testosterone, and aminogluthetamide.

79. (New) The dimeric antibody of claim 38, wherein said cytotoxic agent is a prodrug selected from the group consisting of phosphate-containing prodrugs, thiophosphate-containing prodrugs, sulfate containing prodrugs, peptide containing prodrugs, β -lactam-containing prodrugs, optionally substituted phenoxyacetamide-containing prodrugs, optionally substituted phenylacetamide-containing prodrugs, 5-fluorocytosinem, and 5-fluorouridine prodrugs that can be converted to the more active cytotoxic free drug.